25th Multidisciplinary Management of Cancers: A Case-based Approach

CNS Malignancies: A Case-based Approach

Saturday, March 8, 2025 - 1:30 pm

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Panelists

Jennie Taylor, MD, MPH, Faculty, UCSF – Chair
Thomas Nelson, MD, Faculty, UCSF - Case Presenter

Neuro-/Medical Oncology

Orwa Aboud, MD – UC Davis
Antonio Omuro, MD – Stanford
Nancy Rubin, DO - CHOMP

Neurosurgical Oncology

Melanie Hayden Gephart, MD - Stanford
Jacob Young, MD - UCSF

Radiation Oncology

Steve Braunstein, MD, PhD – UCSF
Iris Catrice Gibbs, MD – Stanford
Matt Susko, MD - UCSF

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Disclosures

Faculty Name	Role	Type of Financial Relationship	Company
Jennie Taylor	**Chair**	Advisory Board or Panel	Servier
		Consultant	Mount Sinai Health Systems, University of Colorado and Curio Science
		Grants/Research Support	Servier and BMS
		Other Financial or Material Support (royalties, patents, etc.)	UpToDate
Thomas Nelson	**Junior Faculty**	Disclosed no relevant financial relationships.	
Orwa Aboud	Panelist	Advisory Board or Panel	Servier Pharmacology
		Consultant	MRI math, Adivo Association, General Dynamics, Woltera Kluwer, and Sago
Steve Braunstein	Panelist	Disclosed no relevant financial relationships.	
Melanie Hayden Gephart	Panelist	Advisory Board or Panel	SensoBrain and Telix
		Grants/Research Support	Quadriga
		Stock/Shareholder (excluding diversified mutual funds)	SmartLens
Iris Catrice Gibbs	Panelist	Disclosed no relevant financial relationships.	
Antonio Omuro	Panelist	Advisory Board or Panel	Ono Pharma, Nurix, Telix, Servier, and Curevac
		Grants/Research Support	Arcus Biosciences
Nancy Rubin	Panelist	Disclosed no relevant financial relationships.	
Matt Susko	Panelist	Disclosed no relevant financial relationships.	
Jacob Young	Panelist	Disclosed no relevant financial relationships.	

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ANCO and i3 Health have mitigated all relevant financial relationships.

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Acknowledgements

This presentation was made possible by contributions from panelists and our patients.

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Learning Objectives

1. Understand clinical implications of molecular alterations in CNS tumors
2. Discuss evidence-based and practical management of brain tumors
3. Describe imaging-based response assessment of brain tumors
4. Recognize indications for seizure prophylaxis
5. Discuss management for disease- and treatment-related symptoms

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Overview

- Case 1: Enhancing left frontal mass; discussion of management and updated response assessment criteria
- Case 2: Non-enhancing right parietal mass; clinical applications for molecular testing and seizure management
- Case 3: Enhancing left temporal mass; management in elderly and edema
- Case 4: Enhancing right temporal mass; management of leptomeningeal disease

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Case 1: A Heterogeneously Enhancing Left Frontal Lobe Mass

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Case 1: History

A 65-year-old woman seeks neurologic care for ~1 year of photophobia with more recent subjective eye movement difficulties leading to trouble with reading. Initial examination by outside neurologist was reportedly reassuring. Due to symptom persistence, MRI brain was obtained 6 months later.

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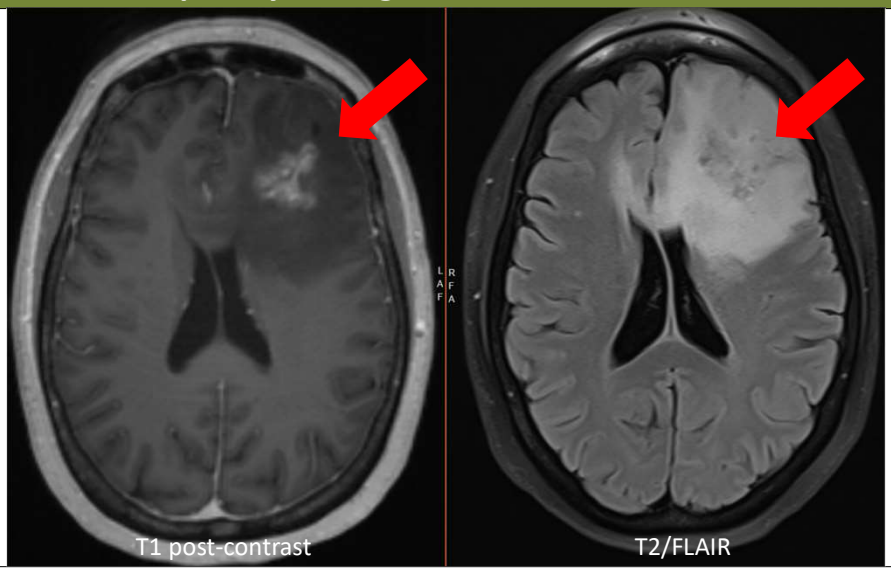

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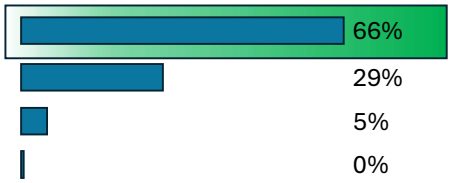
Question 1.1

Based on prior imaging, patient demographics, and history, which of the following is most likely?

a. Glioblastoma, IDH wildtype
b. Astrocytoma, IDH mutant
c. Meningioma
d. Metastasis



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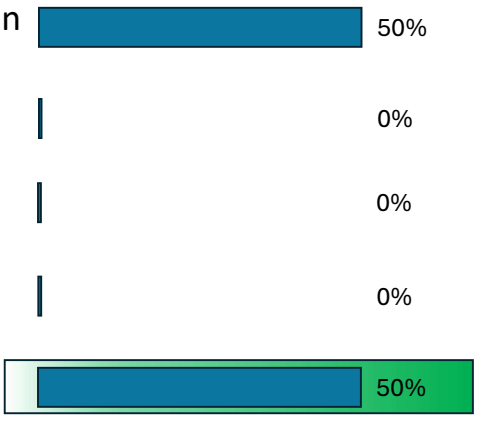
Question 1.2

What would be recommended surgical approach?

a. Biopsy first followed by resection depending on pathology
b. Resection of contrast enhancing disease with the patient asleep
c. Resection of contrast enhancing and FLAIR disease with the patient asleep
d. Resection of contrast enhancing disease with the patient awake
e. Resection of contrast enhancing and FLAIR disease with the patient awake



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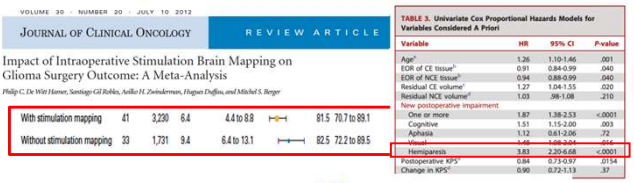
Surgical Technologies Exist to Improve Extent of Resection and Make it Safer

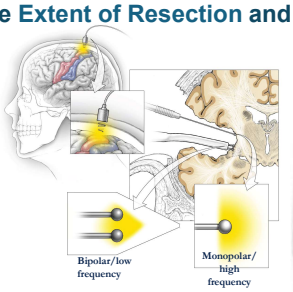

JOURNAL OF CLINICAL ONCOLOGY — REVIEW ARTICLE

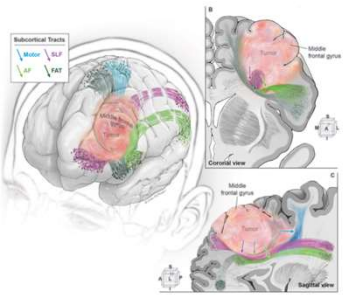
Impact of Intraoperative Stimulation Brain Mapping on Glioma Surgery Outcome: A Meta-Analysis

With stimulation mapping	41	3,230	6.4	4.4 to 8.8	81.5 70.7 to 89.1
Without stimulation mapping	33	1,731	9.4	6.4 to 13.1	82.5 72.2 to 89.5

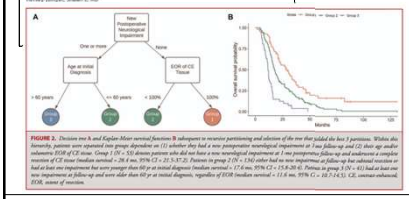
TABLE 3. Univariate Cox Proportional Hazards Models for Variables Considered A Priori

Variable	HR	95% CI	P-value
Age	1.26	1.10-1.46	.001
EOR of CE tissue	0.91	0.84-0.99	.040
EOR of NCE tissue	0.94	0.88-0.99	.040
Residual CE volume	1.27	1.04-1.55	.020
Residual NCE volume	1.03	.98-1.08	.210
New postoperative impairment			
One or more	1.87	1.38-2.53	<.0001
Cognitive	1.51	1.15-2.00	.003
Aphasia	1.12	0.61-2.06	.72
Visual	1.45	1.08-2.04	.016
Hemiparesis	3.83	2.20-6.68	<.0001
Postoperative KPS	0.84	0.73-0.97	.0154
Change in KPS	0.90	0.72-1.13	.37





Association of Neurological Impairment on the Relative Benefit of Maximal Extent of Resection in Chemoradiation-Treated Newly Diagnosed Isocitrate Dehydrogenase Wild-Type Glioblastoma



JNS

The effects of new or worsened postoperative neurological deficits on survival of patients with glioblastoma

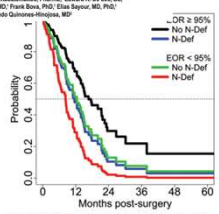
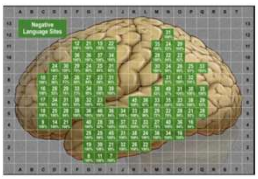


FIG. 3. Predicted overall survival by EOR and presence of a new post-operative neurological deficit (N-Def). Patients who had an EOR of ≥ 95% with a postoperative neurological deficit had very similar survival as patients who had an EOR of < 95% without a postoperative neurological deficit.



THE NEW ENGLAND JOURNAL OF MEDICINE

Functional Outcome after Language Mapping for Glioma Resection

Nader Sanai, M.D., Zaman Mirzadeh, Ph.D., and Mitchel S. Berger, M.D.

De Witt Hamer et al, JCO, 2012
Aabedi et al, Neurosurg, 2022
M Rahman et al, J Neurosurg, 2016
N Sanai et al, NEJM, 2008

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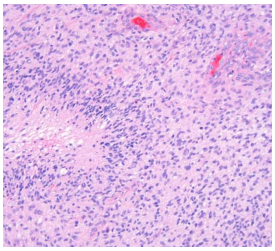
Case 1: Diagnosis of Astrocytoma, IDH-mutant, WHO grade 4

She underwent subtotal resection at outside hospital with pathology demonstrating:

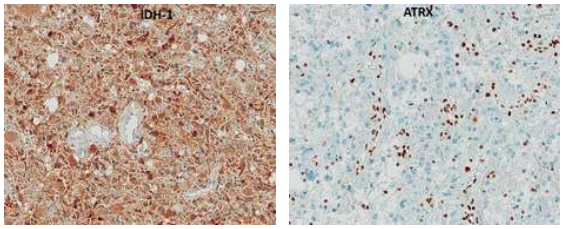
"…[A] moderately cellular, moderately pleomorphic glial neoplasm with extensive infarct-like necrosis… as well as focal microvascular proliferation. Mitotic figures are rare.

Immunostains show the following:

- GFAP (diffusely positive), **IDH-1 p.R132H positive**
- p53 negative, ATRX nuclear loss, SOX10 rare
- Ki-67 of up to 3.3%. **MGMT promoter methylated.**"



Pseudo-palisading necrosis with microvascular proliferation[1]



IHC staining for IDH-1 mutation and ATRX mutation[2]

[1]*Wood et al, Diagn Pathol, 2019*
[2]*Lee et al, Acta Neuropathol Commun, 2017*

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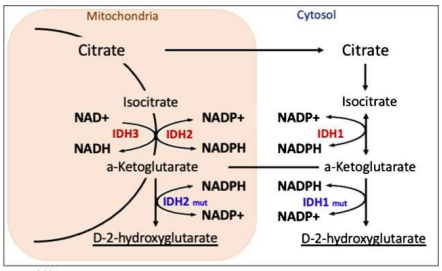
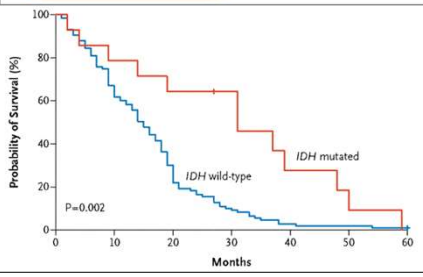
Case 1: Clinical Significance of IDH Mutation

- Disruption of IDH1 function in TCA cycle leads to accumulation of 2-hydroxyglutarate (2-HG)[1,2]
- 2-HG may then activate NMDA receptors, yielding epileptogenesis (no seizures to date in this patient)[1,2]
- Both predictive and prognostic
- IDH mutation confers significant survival advantage; median OS 31-36 months vs 12-15 months for IDH wildtype[3,4]





[1]Dang et al, Nature, 2009
[2]Alshiekh Nasany et al, Curr Neur and Neurosci Rpts, 2023
[3]Yan et al, NEJM, 2009
[4]Hartmann et al, Acta Neuropath, 2010

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Molecular and Histologic Features in IDH-mutant Tumors

- Criteria for upgrading grade 2 → grade 3 or 4 disease[1,2]

	Grade 4 (any of the below)	Grade 3
Histologic	Necrosis Microvascular proliferation	Higher cellularity Increased nuclear atypia Significant mitotic activity
Molecular	CDKN2A/B homozygous* deletion	

- Although *CDK4* amplification and *RB1* mutation are prognostically similar to CDKN2A/B deletion, these are not sufficient for diagnosis[2]; *MYCN* amplification appears quite deleterious as well[3]
- Similarly, *PICK3R1, PIK3CA,* and *PDGFRA* alterations may be negative prognostically but not yet established for upgrading[1]

*Hemizygous deletion does not worsen OS or PFS[4]

[1]Brat et al, Acta Neuropath 2020
[2]Louis et al, Brain Path, 2020
[3]Lee et al, Sci Rpts, 2023
[4]Ippen et al, Neuro-onc, 2024

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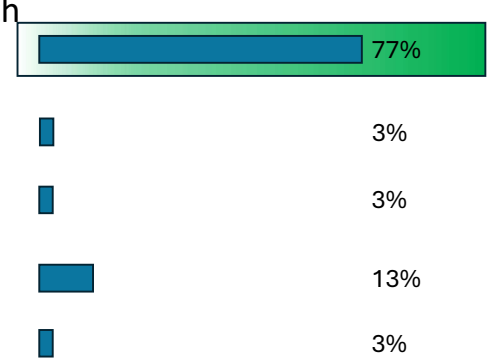
Question 1.3

Presuming this patient has a KPS/ECOG of at least 70/1, recommended standard of care management of this tumor would comprise:

a. Concurrent chemoradiation and adjuvant with temozolomide (TMZ)
b. Radiotherapy followed by procarbazine/CCNU/vincristine (PCV)
c. Temozolomide followed by adjuvant radiotherapy
d. Radiotherapy followed by mIDH inhibitor
e. mIDH inhibitor monotherapy



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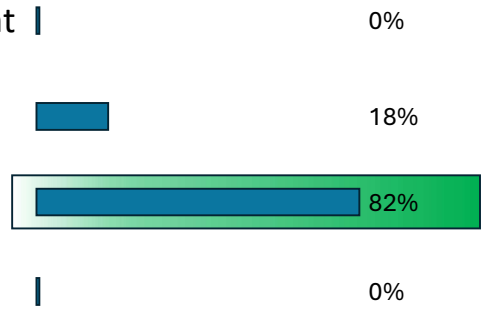
Question 1.4

In which scenario would proton radiotherapy be considered?

a. 76-year-old woman with newly diagnosed right parietal glioblastoma
b. 27-year-old man with recurrent left occipital glioblastoma
c. 41-year-old woman with newly diagnosed left temporal oligodendroglioma, WHO grade 2
d. 65-year-old man with recurrent right frontal glioblastoma



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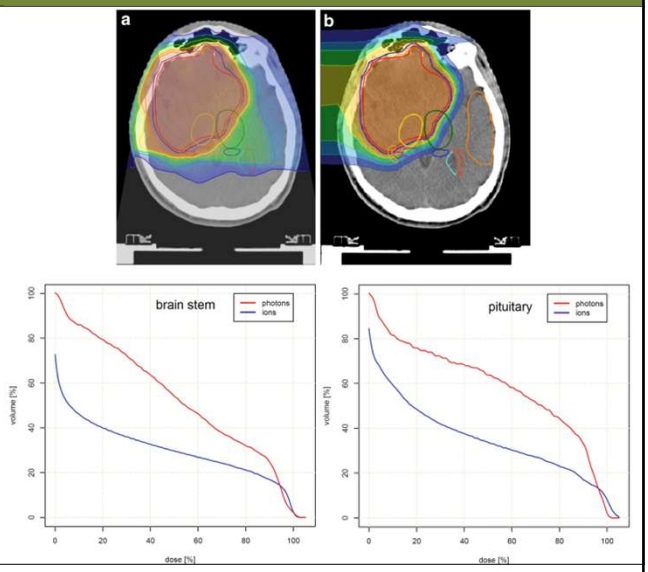
Proton vs Photon Therapy for LGG[1]

Proton therapy delivers radiation in a Bragg Peak, decreasing the integral dose received and protecting adjacent normal tissues

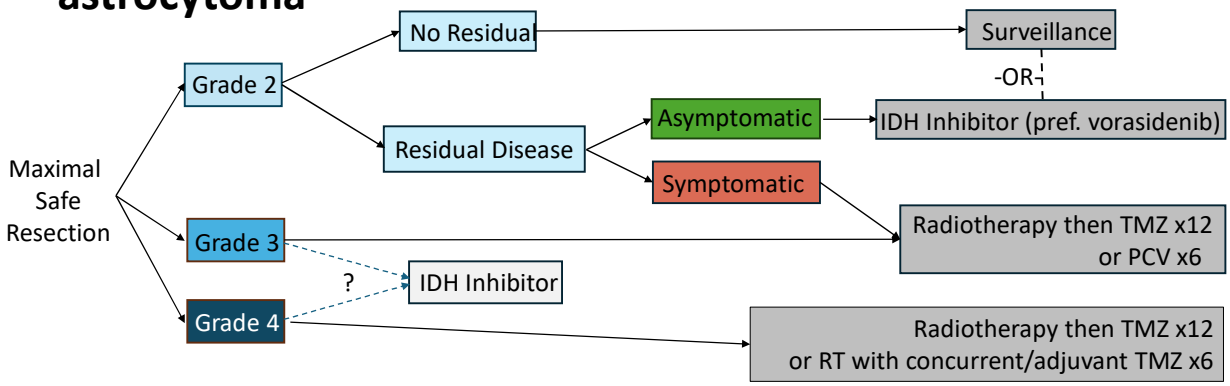
Individuals with LGG have good prognosis and are at risk for long term sequela of radiation therapy, the risk of which could be decreased with proton therapy

These risks include endocrine dysfunction, hearing loss, neurocognitive impairment and the risk for secondary malignancies



[1]*Harrabi et al, Strahlenther Onkol, 2016*

Proposed upfront management of IDH mutant astrocytoma



Adapted from Miller *et al, Neuro Onc, 2023;*
Van den Bent *et al*, *Neuro-oncology,* 2024;
and Nakhate *et al*, *Curr Neur and Neurosci Rpts,* 2024

Case 1: Treatment with Concurrent Chemoradiation

- She received concurrent chemoradiation with temozolomide at 75 mg/m^2
- During first 3 cycles of adjuvant temozolomide, developed increasing headaches, fatigue, and some changes to right-sided fine motor control
- Restarted dexamethasone with some symptomatic benefit, but intolerable insomnia
- Repeat scan reviewed in clinic (next slide)

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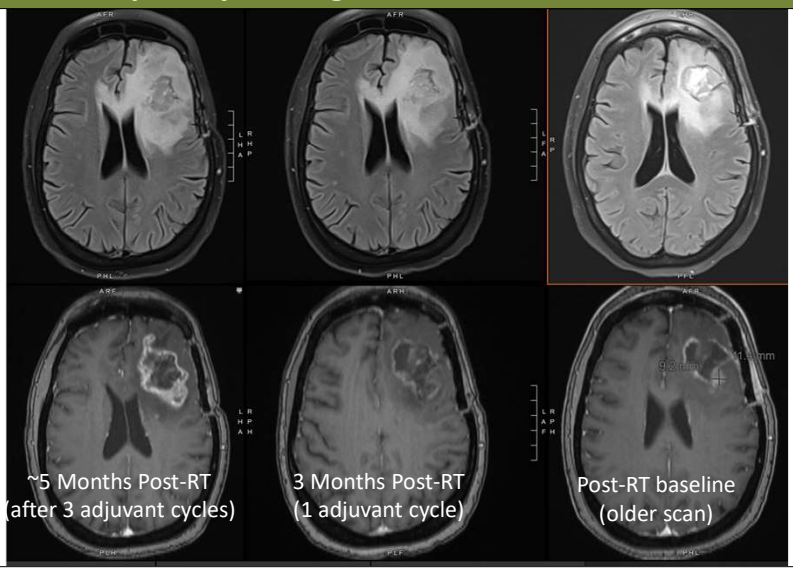

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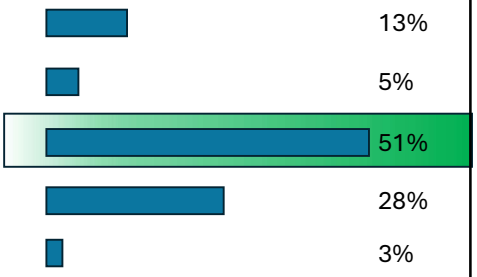
Question 1.5

Given MRI and clinical findings, what would be next course of action?

a. Continue adjuvant TMZ for at least one additional cycle and repeat MRI brain in 4-6 weeks
b. Stop TMZ and start lomustine monotherapy
c. Stop TMZ and start bevacizumab monotherapy +/- lomustine
d. Stop TMZ and start mIDH inhibitor
e. Repeat irradiation



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Response Assessment in Neuro-oncology v2.0

Determining Baseline		Category	Criteria
New Diagnosis	Post-op scan if no RT	Progressive Disease (PD) (“any”/”or”)	New measurable lesion(s), 25%+ increase in sum of diameters, 40%+ increase in volume, new LMD, clinical deterioration, or loss to follow-up
	Post-RT scan if received	Stable Disease (SD) (“and”)	No new lesions, no progression of nonmeasurable or nontarget lesions
Recurrent Disease	Scan just prior to new treatment	Partial Response (PR) (“and”)	50%+ decrease in sum of diameters (or 65%+ decrease in volume), no new lesions, stable corticosteroids, and clinical stability
		Complete Response (CR) (“and”)	Sustained disappearance of lesions, no steroids, and clinical stability

Wen et al, JCO, 2023

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Management of Recurrent Astrocytoma, IDH mutant, Grade 4

- Alkylating agents and nitrosoureas, PCV, and TMZ (if prior durable response)
- Re-resection
- Re-irradiation
- Clinical trials
- mIDH inhibitors

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Select Existing IDH Inhibitor Data (Sparse Grade 4 Results)

Agent	Phase	Year	Num Pts (Gr 4/Total)	Enhancing Response	Non-enhancing response
Ivosidenib[1]	1	2020	12/66	mPFS 1.4 mon (all grades)	mPFS 13.6 mon (all grades)
Vorasidenib[2]	1	2021	4/52	mPFS 1.1 mon	mPFS 36.8 mon (all grades)
Vorasidenib[3]	3	2023	0 (gr 2 only)	N/A	Grade 2 only: ORR 11%, 83% SD mPFS 27.7 mon vs placebo 11.1 mon
Safusidenib[4]	1	2023	7/47	mPFS 10.4 weeks (all grades)	mPFS not reached

[1]*Mellinghoff et al, JCO, 2020*
[2]*Mellinghoff et al, Clin Can Res, 2021*
[3]*Mellinghoff et al, NEJM, 2023*
[4]*Natsume et al, Neuro-onc, 2023*

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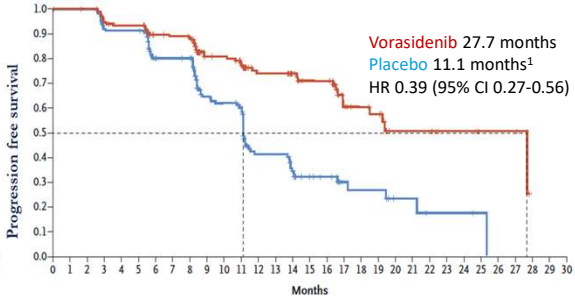
Phase 1/3 Results Imply a Possible Need for Combined Therapy

- IDH inhibitor monotherapy is likely less effective in higher grade (e.g., grade 4) disease; clinical trials investigating this
- Ongoing work will determine if combination therapy is more effective
- It is unknown if limited benefit was seen due to prior trial populations being heavily pretreated

INDIGO: Newly diagnosed IDH-mutant, grade 2



[1]Mellinghoff *et al*, *NEJM*, 2023

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Trials at UCSF for recurrent astrocytoma, IDH mutant

PARP inhibitor therapy with TMZ (non-surgical, PO drug)
- Phase 1/2a for any grade
- At least 6 months since prior alkylating therapy, RT, and bevacizumab

Perioperative pembrolizumab and vorasidenib permutations then combination
- Phase 1 for grade 2 or 3
- Vorasidenib, vorasidenib + pembrolizumab, or neither x4 weeks pre-op

Case 2: A Non-enhancing Parietal Mass

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Case 2: History

A 49-year-old man with baseline right foot numbness and tingling presents to urgent care for similar left-sided symptoms over 4 days. This new numbness produces a limp and imbalance. Symptoms are persistent and potentially increasing in severity. No headache, language difficulties, or vision changes occurred.

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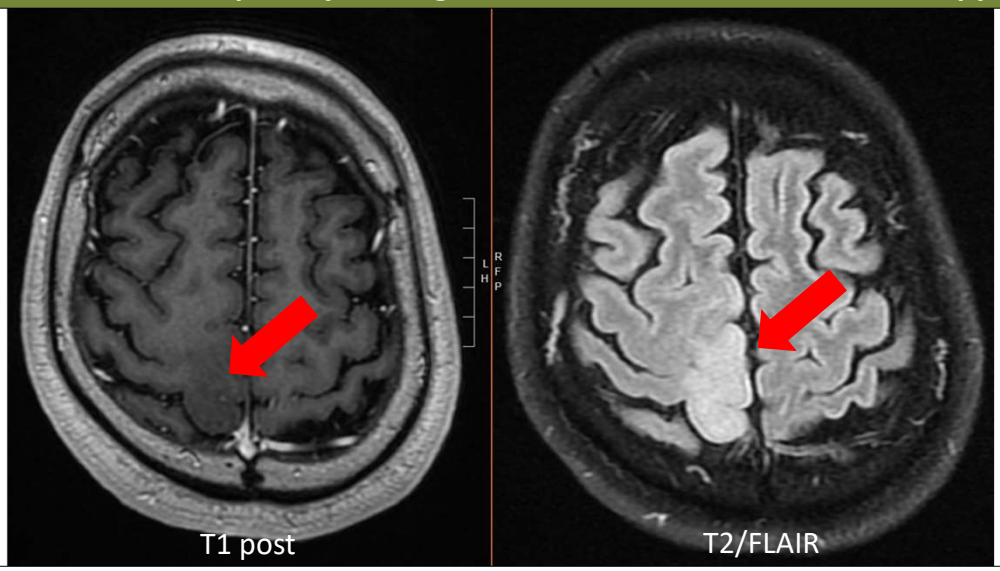

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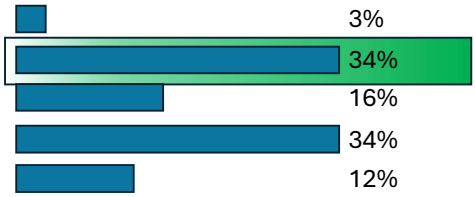
Question 2.1

Based on imaging, patient demographics, and history, which of the following is most likely?

a. Astrocytoma, IDH mutant, WHO grade 4
b. Astrocytoma, IDH mutant, WHO grade 2
c. Oligodendroglioma, IDH mutant, WHO grade 3
d. Oligodendroglioma, IDH mutant, WHO grade 2
e. Glioblastoma, IDH wildtype, WHO grade 4



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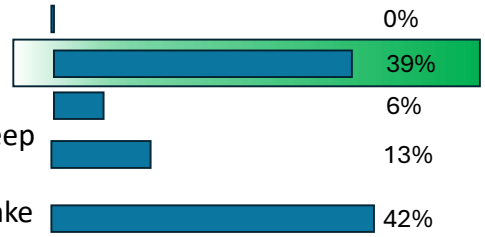
Question 2.2

What would be your surgical plan?

a. Observation with serial imaging
b. Biopsy only
c. Biopsy + Laser Induced Thermal Therapy (LITT)
d. Resection of the FLAIR disease with the patient asleep with motor mapping
e. Resection of the FLAIR disease with the patient awake with motor mapping



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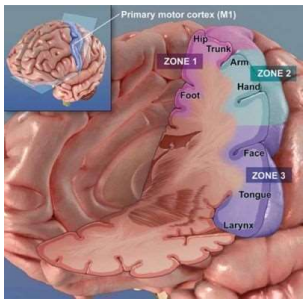
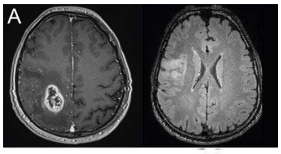
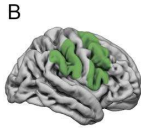
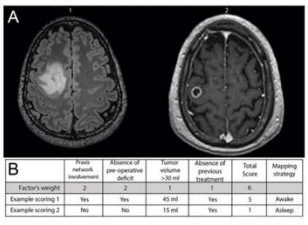
Evolving Management of Motor Cortex Lesions: Awake or Asleep resection? LITT?



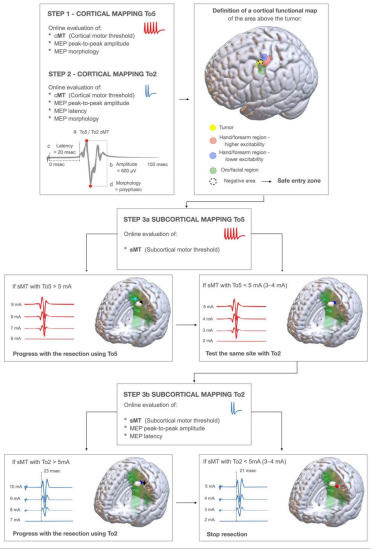
Magill *et al*, *J Neurosurg*, 2017







Rossi *et al*, *J Neurosurg*, 2022



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Case 2: Biopsy with Unclear Histology

Biopsy was undertaken and pathology reviewed at an outside hospital. The description includes:

"…pleomorphic cells infiltrating through benign brain parenchyma… giant cell component and eosinophilic granular bodies are **not** identified. There is **one area with early apoptosis suggestive of possible early necrosis,** but well-developed palisading necrosis is not identified. **No vascular proliferation is appreciated.** IDH-1 R132H wildtype."

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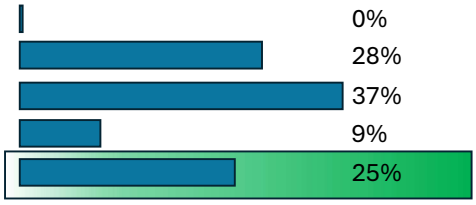
Question 2.3

In light of the reported histology, what is the diagnosis?

a. Astrocytoma, IDH mutant, WHO grade 4
b. Astrocytoma, IDH mutant, WHO grade 2
c. Astrocytoma, IDH wildtype, WHO grade 3
d. Glioblastoma, IDH wildtype, WHO grade 4
e. Additional testing is needed



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Case 2: Molecular Characterization

Identified	Not Identified
CDKN2A/B homozygous deletion	**TERT promoter mutation**
PTPRZ1::MET fusion	**EGFR amplification**
MGMT promoter methylation	H3 G34R
Ch 7 gain	BRAF
Partial Ch 10 loss	**IDH-1/2**
	EGFR
	FGFR-1/2/3

WHO 2021 diagnosis: glioblastoma, IDH wildtype, WHO grade 4

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Case 2: Molecular Glioblastoma Features

As proposed in cIMPACT-NOW (updates 3 and 6)[1,2] and implemented in WHO CNS 2021:[3]
***Any* of the following are sufficient for diagnosis of glioblastoma** in IDH-wildtype, H3-wildtype astrocytomas:

- *EGFR* amplification
- *TERT* promoter mutation
- Concurrent whole gain of chromosome 7 and loss of chromosome 10

It does not appear that molecular-only GBM has a notable difference in outcomes[4]

[1]*Brat et al, Acta Neuropath, 2018*
[2]*Louis et al, Brain Pathol, 2020*
[3]*Louis et al, Neuro-onc, 2021*
[4]*Papacocea et al, Int J Mol Sci, 2024*

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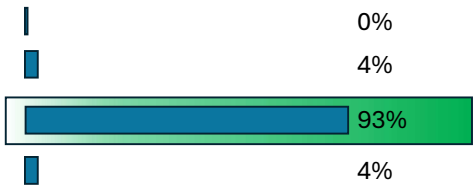
Question 2.4

What upfront management would you consider in this situation?

a. Observation with short interval (4-6 weeks) MRI brain
b. Adjuvant TMZ monotherapy +/- TTF
c. Concurrent chemoradiation followed by adjuvant TMZ +/- TTF
d. Adjuvant radiation monotherapy +/- TTF



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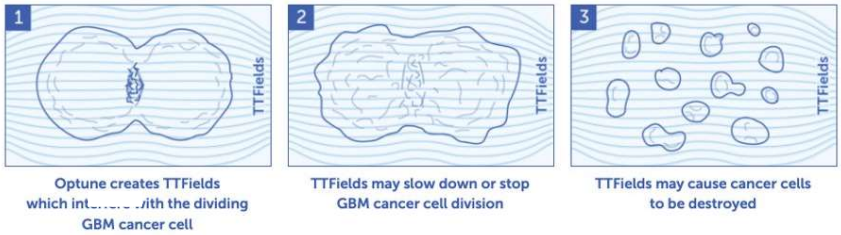
A Discussion of Tumor Treating Fields (TTFs)

	TMZ alone	TMZ + TTFs
Median OS (months, 95% CI)	16.0 (14.0-18.4)	20.9 (19.3-22.7)
5-year survival (%, 95% CI)	5% (2-11%)	13% (9-18%)

Stupp *et al*, *JAMA*, 2018



Slide courtesy of MMC 2022 team

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Case 2: Upfront Treatment

Patient proceeded with concurrent chemoradiation with temozolomide at 75 mg/m^2

One day into radiotherapy, he developed left leg stiffening that abated in 20-30 seconds concerning for seizure

Initiation of levetiracetam 500 mg BID, but recurrent episode one week later

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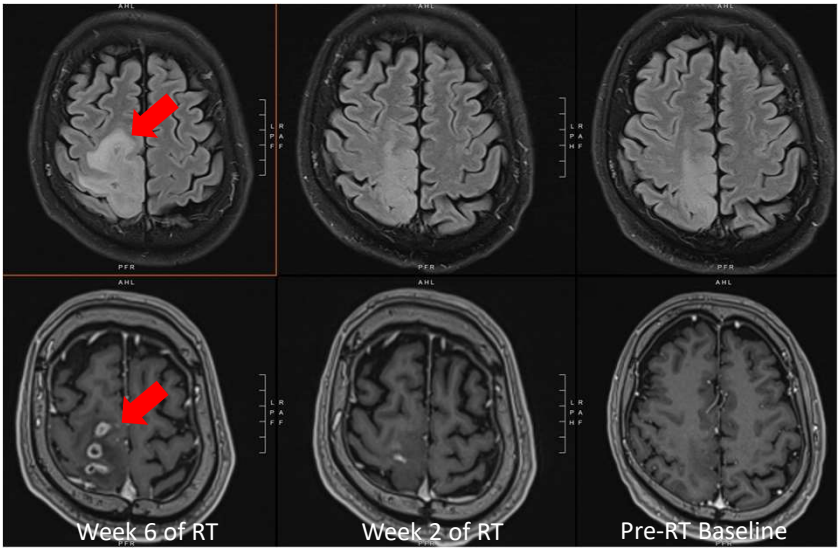

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Question 2.5

Based on imaging and symptomatology, what does the imaging change likely represent and what are your recommendations?

a. Pseudoprogression - finish radiation and concurrent TMZ, monitor with post-RT MRI, then proceed with adjuvant TMZ — 0%
b. Early progression - consider aggressive resection then re-irradiation — 0%
c. Early progression - taper dexamethasone and proceed with adjuvant TMZ at 150 mg/m^2 — 0%
d. Pseudoprogression - consider 1-3 treatments with bevacizumab then proceed with adjuvant TMZ — 0%

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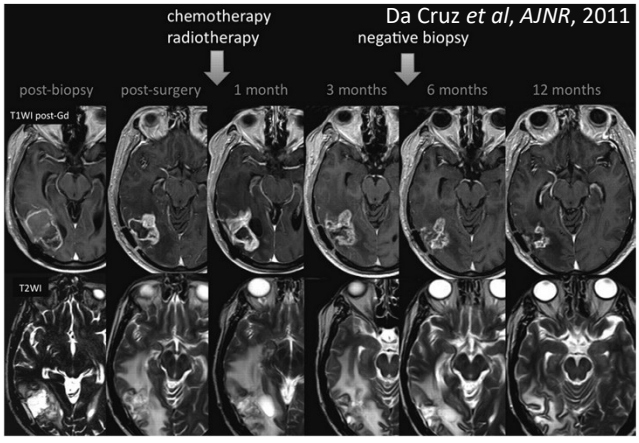
Case 2: Suspicion for Pseudoprogression

- New enhancement during and shortly after RT can be pseudoprogression or disease-related[1,2]
- MGMT promoter methylation confers an increased risk[3]
- Bevacizumab 5-10 mg/kg every 2-4 weeks useful if symptomatic
- Per RANO 2.0
  - Imaging changes concerning for progression ***within 12 weeks of RT end*** require confirmation scan 4 weeks later
  - Short interval MRI must show ongoing (≥ 25%) increase in enhancement for progression



[1]Brandes *et al, JCO,* 2008
[2]Da Cruz *et al, AJNR,* 2011
[3]Brandes *et al*, *JCO*, 2008

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Case 2: Bevacizumab Leads to Symptom Improvement

- One infusion yielded significant improvement in seizures
- Radiographic response also seen (next slide)
- Transition to acute rehabilitation and plan for adjuvant TMZ
- Should subsequent MRI be concerning for progression, can consider trial or second-line therapy (e.g., lomustine)

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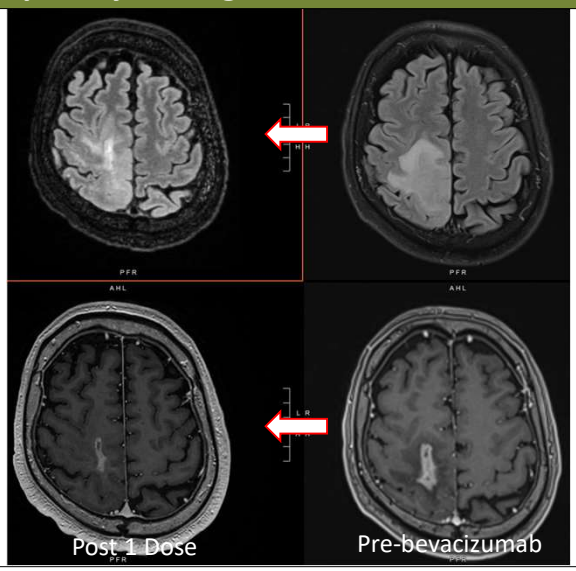

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Case 3: Left Temporal Lobe Mass

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Case 3: History

An 82-year-old woman with diabetes, hypertension, chronic kidney disease, and hearing loss develops subacute cognitive concerns.

Family report behavioral changes like apathy; apraxia; right-sided incoordination; and aphasia. Following evaluation by a neurologist, imaging ordered

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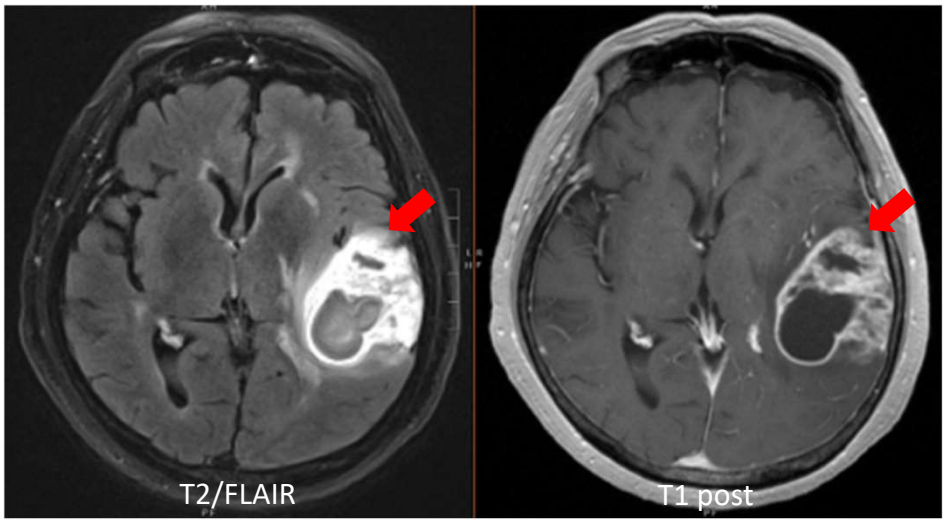

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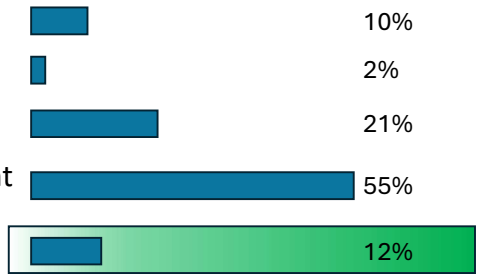
Question 3.1

What would be the initial surgical strategy?

a. Biopsy only
b. Biopsy with LITT
c. Resection of the enhancing disease only with the patient asleep with motor mapping
d. Resection of the enhancing disease with the patient awake with language and motor mapping
e. Any of the above



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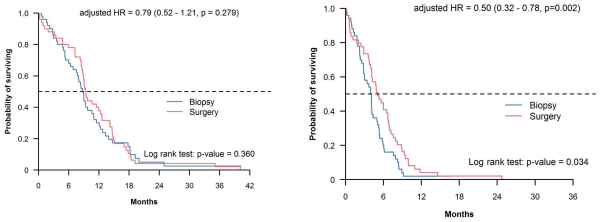
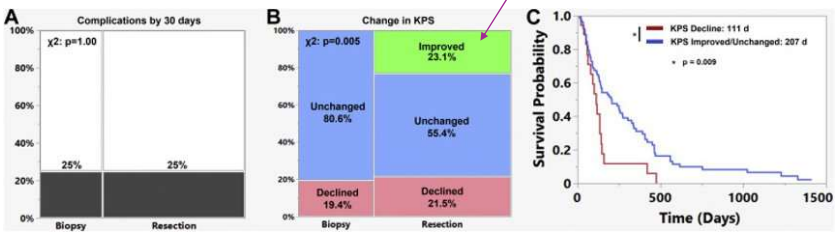
Surgery versus biopsy for elderly patients

Improved QOL in the group undergoing surgery



Surgery versus biopsy for frail patients

Laigle-Donadey *et al, J Neurosurg,* 2022



Morshed *et al, J World Neurosurg,* 2022

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Case 3: Glioblastoma was confirmed on biopsy

Biopsy confirmed glioblastoma

Post-surgery, functional decline with worse communication, instability, right-sided weakness, and fatigue

On referral, family was unsure what treatment, if any, would be appropriate

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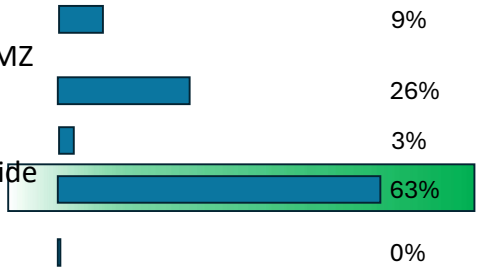
Question 3.2

Which of the following would likely **not** be preferred for upfront management?

a. Chemoradiation to 40.05 Gy in 15 fractions with temozolomide at 75 mg/m2 followed by adjuvant TMZ
b. Temozolomide monotherapy
c. Radiation monotherapy
d. Chemoradiation to 60 Gy in 30 fractions with temozolomide at 75 mg/m2 followed by adjuvant TMZ
e. Referral to palliative care



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Management of Glioblastoma in the Elderly (> 70 years)

Influenced by performance status

Radiotherapy is typically the backbone

Role of temozolomide (concurrent or adjuvant) based on MGMT promoter methylation and functional status

If unable to receive radiation, TMZ monotherapy can be considered for methylated patients

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Phase 3 Data Support RT +/- TMZ

The Nordic study demonstrated the toxicity of standard 6-week radiation in the elderly[1], and TMZ or RT monotherapy was found comparable in NOA-08[2]

Perry *et* al showed a survival benefit of adding TMZ to hypofractionated RT (mOS 9.3 mons with TMZ v 7.6 months without)[2]

Patients lacking MGMT promoter methylation, benefit of TMZ is less certain; reanalysis of NOA-08 and Nordic data support omission[3,4]

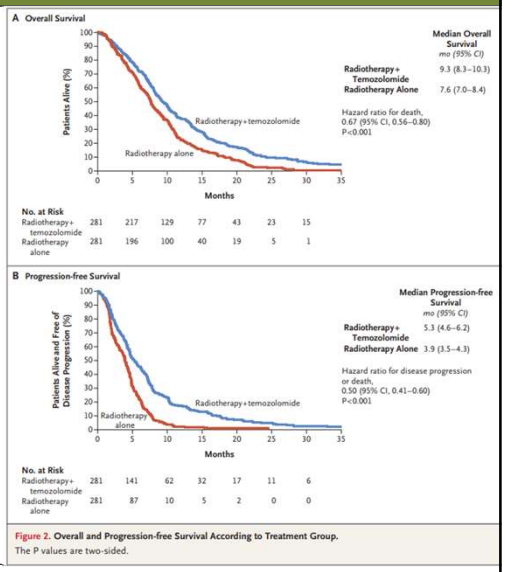

Figure 2. Overall and Progression-free Survival According to Treatment Group.
The P values are two-sided.

[1]Malmström *et al*, *Lancet Onc*, 2012
[2]Wick *et al*, *Lancet Onc*, 2012
[3]Perry *et al*, *NEJM*, 2017
[4]Hegi *et al*, *Neuro-onc*, 2024

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Case 3: A Trial of Upfront Symptom Management

Given the patient's significant fatigue and suspicion that many symptoms were driven by local mass effects (without prospect of robust debulking), elected to start dexamethasone 4 mg daily

She felt much better and was able to taper within two weeks

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Steroid Management Recommendations

Corticosteroids (typically dexamethasone) are indicated for symptomatic edema[1]

In highly symptomatic patients, a "pulse" dose of 10-20 mg can be considered

Dosing is typically 1-16 mg in divided doses; higher doses likely lack additional benefit but increase risk for adverse events[2]

Goal is minimal effective dose for shortest period possible

Indefinite corticosteroid use, or in asymptomatic patients, is not indicated

[1]Dietrich *et al*, *Exp Rev Clin Pharm*, 2011
[2]Jessurun *et al*, *J Neuro-onc*, 2019

Case 4: A Right Temporal Lobe Mass

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Case 4: A Young Woman with New Headache and Nausea

35-year-old woman with known metastatic cervical squamous cell carcinoma, diagnosed after abnormal vaginal bleeding during pregnancy evaluation ~6 years prior, presents with new headache and nausea.

Treatment history:

1) Hysterectomy/bilateral salpingo-oophrectomy with sentinal lymph node dissection (+)
2) Chemosensitizing RT to 50 Gy with cisplatin. Carboplatin AUC2 was used to bridge back to cisplatin.

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Case 4: Systemic Recurrence with Response to Chemo

First recurrence at the ureter, vaginal apex, and hilar lymph node was noted 8 months later and treated with carboplatin, paclitaxel, and bevacizumab x6 cycles.

Post-chemo PET/CT showed improvement. Bevacizumab monotherapy was continued with disease control but stopped due to poor wound healing after a skin lesion removal.

Head imaging in work-up of new headache and nausea was obtained.

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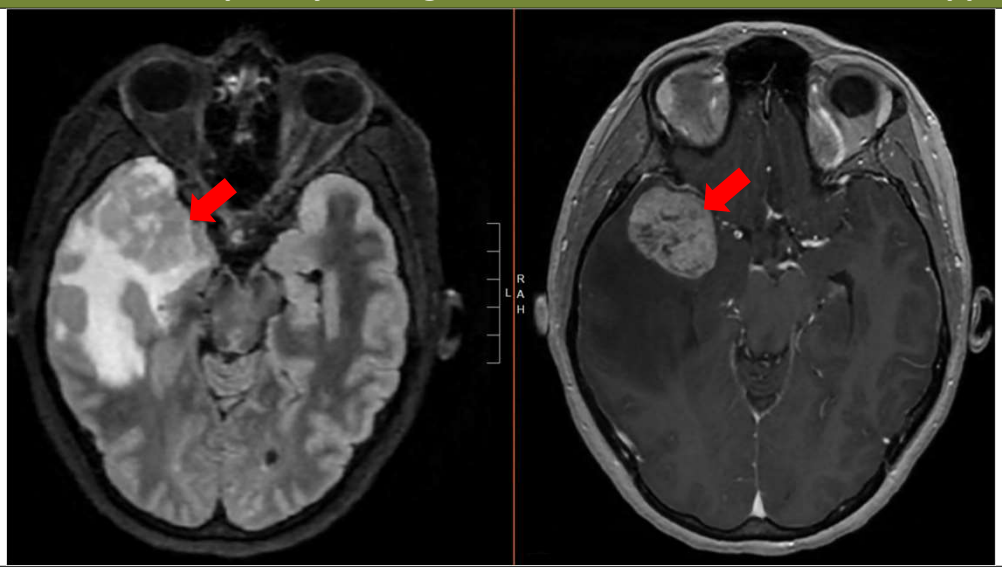

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Question 4.1

What is the most likely etiology based on this imaging in the setting of stable systemic disease?

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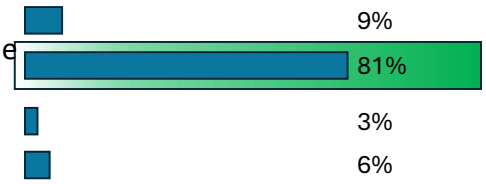
Question 4.2

What is your plan for local management of this brain lesion?

a. Pre-operative SRS followed by resection
b. En bloc resection followed by fractionated RT to the surgical bed with margin
c. Biopsy with LITT
d. Biopsy followed by fractionated RT



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25th Multidisciplinary Management of Cancers: A Case-based Approach

Case 4: Systemic Recurrence with Response to Chemo

Transferred to UCSF for resection

Pathology: non-keratinizing SCC

FINAL PATHOLOGIC DIAGNOSIS

A. Brain, right temporal mass, resection: Metastatic non-keratinizing squamous cell carcinoma; see comment.

B. Brain, CUSA contents, resection: Metastatic non-keratinizing squamous cell carcinoma; see comment.

COMMENT:
Sections reveal non-keratinizing nests of neoplastic cells with nuclear hyperchromasia, prominent central nucleoli, and moderate eosinophilic cytoplasm. The tumor shows brisk mitotic activity and frequent areas of "dirty" necrosis.

Immunohistochemical stains performed at UCSF Medical Center on block # show the following:
- CK7: Diffuse positivity.
- CK20: Negative in tumor cells.
- CK5/6: Extensive positivity.
- p16: Extensive positivity.
- p63: Extensive nuclear positivity.
- p40: Extensive nuclear positivity.

Overall, the findings are those of a metastatic non-keratinizing squamous cell carcinoma

```
VARIANT: AKT2 p.E17K
TRANSCRIPT ID: NM_001626.4
CLASSIFICATION: Pathogenic
READS: 1574
MUTANT ALLELE FREQUENCY: 55%

VARIANT: CHD2 c.295-1G>C
TRANSCRIPT ID: NM_001271.3
CLASSIFICATION: Pathogenic
READS: 1210
MUTANT ALLELE FREQUENCY: 69%

VARIANT: PBRM1 homozygous/biallelic deletion
TRANSCRIPT ID: All
CLASSIFICATION: Pathogenic
READS: N/A
MUTANT ALLELE FREQUENCY: N/A
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Case 4: Systemic Recurrence with Response to Chemo

Following RT, she began pembrolizumab with no evidence of intracranial or systemic disease.

9 months later: she noted right gluteal pain radiating down the right leg that evolved to saddle anesthesia with urinary and bowel incontinence.

She underwent MRI of lumbar spine

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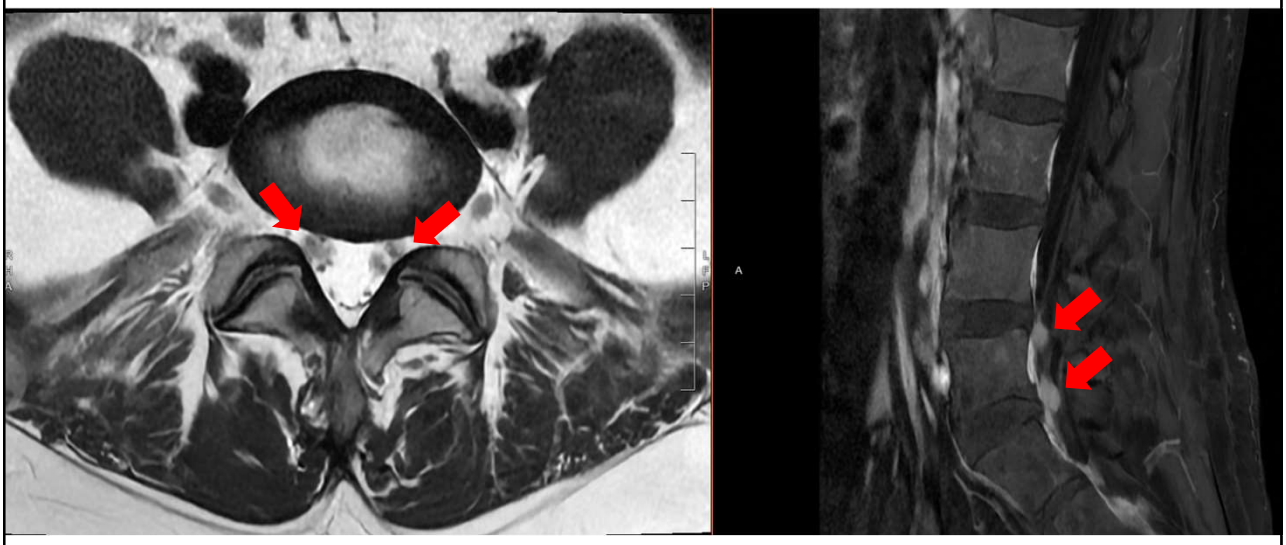

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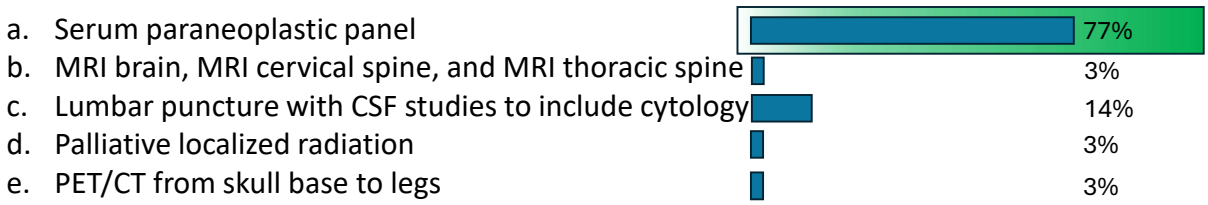
Question 4.3

Based on this imaging, which of the following is **not** clearly indicated?



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Case 4: Local Management of Lumbosacral Leptomeningeal Metastasis

Received palliative radiation with improvement in pelvic symptoms

Unfortunately, she developed intractable headache approximately one week later

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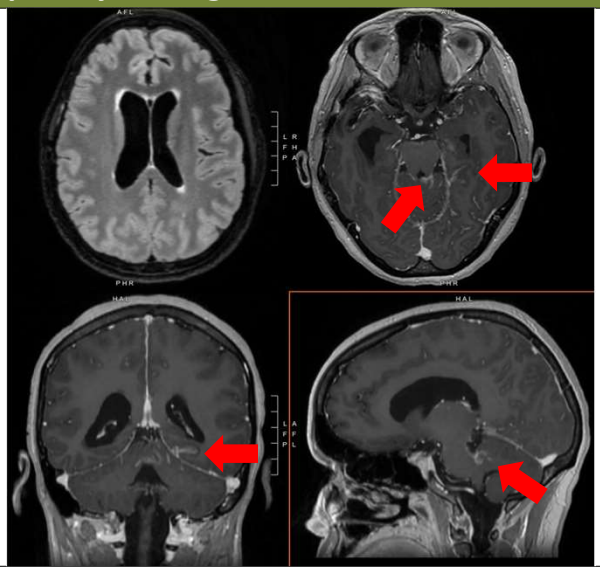

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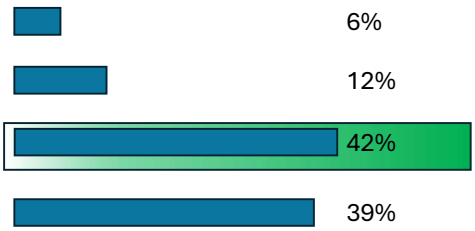
Question 4.4

In the setting of leptomeningeal metastasis involving the brain and cauda, this patient may benefit from which of the following?

a. Focal, hypofractionated radiation to 40 Gy
b. Ventriculoperitoneal shunting and whole brain radiation
c. Ventriculoperitoneal shunting with craniospinal radiation
d. Whole brain radiation and topiramate



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Balancing Quality and Quantity of Life

Leptomeningeal disease (LMD) remains incurable and significantly shortens survival

Increasingly effective systemic therapies may contribute to rising cases of brain metastasis and LMD as late stage complication of disease

VP shunting for non-obstructive hydrocephalus is can improve symptoms, but also delay initiation of therapy including radiation; endoscopic third ventriculostomy offers the same for obstructive cases

Shared medical decision-making can guide individualized therapies for these patients[1]

[1]Lamba et al, *J Neuro-onc*, 2018

Thank you to our panelists, organizers, and audience for their time and participation!

And thank you to our patients for allowing us to learn from their experiences.